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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/408,396	09/29/1999	CHRIS BUHR	GLIS-0128	4009

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JOSEPH LUCCI  
WOODCOCK WASHBURN KURTZ MACKIEWICZ  
& NORRIS LLP  
ONE LIBERTY PLACE 46TH FLOOR  
PHILADELPHIA, PA 19103

EXAMINER

OWENS JR, HOWARD V

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 07/30/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/408,396

**Applicant(s)**

BUHR ET AL.

**Examiner**

Howard V Owens

**Art Unit**

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2001.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-8 is/are allowed.
- 6) ☒ Claim(s) 9-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other:  |

Reissue Application

The following is in response to the request for continued examination filed 7/03/02:

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(a) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/26/02 has been entered.

An action on the merits of claims 1-26 is contained herein below. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Allowable Subject Matter**

Claims 1-8 contain allowable subject matter over the prior art of record.

**35 U.S.C. 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gait, *Oligonucleotide Synthesis: A practical approach*, October 1984, in combination with Montgomery et al., *Journal of Medicinal Chem.*, vol.29 (11), 1986 and Perlman, J. of Med. Chem., vol. 28, 1985, Greene et al., *Protective Groups in Organic Chemistry*, pp. 413-416, 1991.

In claims 9-19, a 2-Deoxy-2-fluoro- -D-arabinofuranosyl with either a protected purine or pyrimidine is set forth. The compounds differ only through the protected exocyclic amines or the ether groups of the analog. The protecting agents used for the purines are benzoyl for adenine and cytosine and isobutyryl for guanine. The protecting group used for the ethers is 4,4-dimethoxytrityl.

Montgomery sets forth the analogous 2-Deoxy-2-fluoro- -D-arabinofuranosyl compound set forth in claims 9-19 when the base is a purine (p. 2390). Perlman sets forth the analogous 2-Deoxy-2-fluoro- -D-arabinofuranosyl compound set forth in claims 9-19 when the base is a pyrimidine (p.743). However, neither Montgomery nor Perlman teach the compound with the appropriate protecting groups for the exocyclic amine or ether moieties. Both Gait and Greene provide the nexus between applicant's invention and the prior art as it teaches the protection of exocyclic amino groups of heterocyclic bases via the use of the protecting group benzoyl for adenine and cytosine, and isobutyryl for guanine in oligonucleotide synthesis. Gait also teaches the use of dimethoxytrityl protecting groups for the temporary protection of the 5' hydroxyl group or an ether moiety during oligonucleotide synthesis (p. 12, paragraph 1 and p. 23, paragraph 1). Greene et al. teach the use of t-butyldimethylsilyl (TBMS) as a protecting agent for 5' hydroxyl groups/ethers.

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It would have been *prima facie* obvious to use protecting groups for exocyclic amines and ethers in a purine or pyrimidine substituted 2-Deoxy-2-fluoro- -D-arabinofuranosyl analog known in the prior art..

One of skill in the art would have been motivated to use known protecting agents such as benzoyl, isobutyryl and dimethoxytrityl agents for exocyclic amines of heterocyclic bases or ether moieties given the use of these protecting agents for said moieties in oligonucleotide synthesis.

Applicant argues that because the Montgomery reference teaches "purine", the Montgomery reference fails to teach, *inter alia*, the base adenine. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

In determining the scope of the prior art, one of skill in the art would clearly recognize that the scope of Montgomery with regards to the term purine is inclusive of known purine bases such as adenine; moreover, on p. 2390 of Montgomery adenine is clearly sets forth as the base component of the nucleoside derivative. Given that the scope of Montgomery is clearly inclusive of adenine as a base for the nucleoside derivative, the teachings of Gait with regard to protecting groups of nucleoside moieties is applicable.

In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of

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ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The rejection of record is based on the combined teachings of Gait, Montgomery and Greene, wherein these references antedate applicant's filing date; moreover, applicant has not shown specifically why the motivation provided by the examiner in view of the prior art is not proper. A statement that there is no motivation provided by the prior art does not fulfill applicant's burden of showing why the motivation is improper nor founded in reasonable scientific principles.

The rejection of claims 20-26 under 35 U.S.C. § 103 as being unpatentable over Gait, *Oligonucleotide Synthesis: A practical approach*, October, 1984 in combination with Sterzycki et al., EP 0316017 A2 is maintained for the reasons of record.

Claims 20-26 are drawn to a modified oligonucleotide or derivative thereof comprising at least one nucleoside selected from the group consisting of an arabinonucleoside and a 2'-deoxy-2'-fluoro -arabinonucleoside.

Sterzycki et al. teach 2'-deoxy-2'-fluoro-arabinonucleosides and derivatives thereof (pp. 2 and 8-10). However, Sterzycki et al. does not teach the formation of oligonucleotide formation from the 2'-deoxy-2' fluoro-arabinonucleosides. The formation of oligonucleotides from nucleoside compounds is well known in the art. Gait teaches the synthesis of oligodeoxynucleotides from deoxyribonucleosides as well as the phosphorothiate and phosphoramidite internucleotide linkages.

It would have been prima facie obvious to synthesize an oligonucleotide from a modified 2'-deoxy-2'-fluoro-deoxyoligonucleotide or derivative thereof, be it arabinose or ribose as the sugar moiety.

A person of ordinary skill in the art would have been motivated to produce the oligonucleotides from deoxynucleosides of the instant claims for the art recognized benefit of the construction, selection and determination of the DNA sequence of recombinants or site directed mutagenesis. One of skill in the art would have been further motivated to use an arabinonucleoside per the teachings of Sterzycki wherein 2'

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derivatives of arabinonucleosides possess antiviral, anitneoplastic and antimetabolic activities (p. 10, lines 1-54).

Applicant has broadly set forth classes of nucleoside compounds which as instantly claimed do not particularly denote novel compounds. Moreover, given the state of the art with regards to the synthesis of oligonucleotides, one of skill in the art would have a reasonable expectation of success in the formation of oligonucleotides from the broad classes of compounds set forth in the instant claims.

Applicant asserts that the "office action does not provide a compelling reason for the combination of Sproat or Sterzycki. However, other than this statement, applicant to date has not provided a rationale as to why the examiner's motivation is not compelling. As cited in the previous action, applicant claimed that the motivation provided by the examiner is "simply not credible". Other than the statement that "site directed mutagenesis requires a naturally occurring nucleic acid", applicant has not provided any factual data to support this assertion. One of skill in the art would recognize that synthetic oligonucleotides are also required to alter genes through site directed mutagenesis. The examiner had also queried applicant as to why a motivation founded in a reference which applicant relies on for the construction of the claimed oligonucleotides is not credible; additionally, applicant has not responded to the examiner's statement that assuming *arguendo* that one of skill in the art would not have had the same motivation as the examiner, applicant's specification clearly points out that the state of the art has already provided a motivation for the formation of oligonucleotides from 2'deoxy-2'fluoro-ribonucleotides, p. 4, Ikehara, *Heterocycles*, specifically that these oligonucleotides have a higher affinity to DNA than normal oligodeoxyribonucleotides.

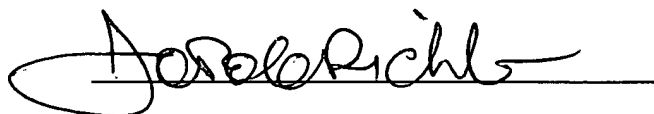
For the reasons stated above, the rejections of record are maintained.

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All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Howard V. Owens  
Patent Examiner  
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A handwritten signature in black ink, appearing to read 'Johann Richter', written over a horizontal line.

Johann Richter, Ph.D., Esq.  
Supervisory Patent Examiner  
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538. The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

The fax phone number for this Group is (703) 308-4556.